CASE REPORT

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Fatal Intoxication Involving Etryptamine

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ABSTRACT: A case of fatal intoxication due to the ingestion of Etryptamine (ethyltryptamine) is reported. Toxicological findings included the following tissue distribution: blood (heart) 5.6 mg/L; urine 80.4 mg/L; vitreous 2.4 mg/L; bile 22.0 mg/L; stomach contents 52.9 mg, brain 16.2 mg/g; liver 18.3 mg/g and kidney 24.0 mg/g. Anatomic pathology showed pulmonary edema and generalized visceral congestion with some epicardial petechiae.

KEYWORDS: toxicology, drugs, etryptamine

Case History

Between 8:30 P.M. and 11:30 P.M. on March 12, 1991, the 19-year-old female victim was alleged to have ingested a glass of beer containing two "hits" of a white powder. She had been told the material was "Ecstasy" (3,4-methylenedioxymethamphetamine). Witnesses to the event described the individual "hits" or doses, as "the size of a dime." She later became disoriented, vomited and eventually went into full cardiac arrest. Resuscitation efforts by others present were unsuccessful. Fire department paramedics were called and subsequently pronounced her dead.

Autopsy Findings

The body was that of a well developed, mildly obese, white female appearing consistent with her stated age of 19 years. External examination was essentially unremarkable with the exception of abraided contusions of both knees and a marked pronation of both feet at the ankles.

Internal examination of the body cavities revealed a 230 g heart with some posterior epicardial petechiae but with no visible occlusive or functional disease. The lungs were edematous and congested, the right lung weighed 650 g and the left, 480 g. The larger of the two airways contained a large quantity of a dark gray, opaque thick liquid. The

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stomach contained 150 cc of a dark gray, semi-liquid, opaque material mixed with a lesser amount of a finely granular lighter colored material. With the exception of the larynx and trachea, which contained material resembling that of the gastric contents, and generalized visceral congestion, all other organ systems were essentially unremarkable.

Laboratory Results

A routine analysis for basic and neutral drugs was performed on 1 mL of heart blood to which was added 200 ng of mepivicaine as an internal standard. The analysis consisted of adjusting the pH of the matrix to approximately 9.5 with 1.5 mL of saturated sodium borate and extracting the buffered mixture with 10 mL of n-butyl chloride. The sample was rotated for 10 min on a rotary mixer and then centrifuged for 10 min at 2500 rpm. The n-butyl chloride supernate was transferred to a 15 mL conical evaporation tube to which was added 50 μL of isoamyl acetate. The solvent was evaporated in a 40°C heating block, under a stream of dry air, to approximately 50 μL. An additional 50 μL of hexane: ethanol (50:50) was added to the evaporated solvent residue, vortexed and 1.5 μL submitted to capillary column gas-liquid chromatography.

The screening analysis and subsequent quantitative analyses were performed on a Hewlett/Packard 5790 gas chromatograph equipped with a 12.5m Ultra 2 (crosslinked 5% phenyl methyl silicone) capillary column, .32 mm i.d. × 0.52 film thickness (Hewlett/Packard) and thermionic (nitrogen/phosphorus detection). A 1:10 split injection technique was employed with injection port and detector temperatures of 225 C and 285 C, respectively. The high purity grade (99.999%) helium carrier gas was operated at a flow rate of 3.3 mL/min with 30 mL/min of detector make-up flow. The initial temperature of 110 was held for 1 min and ramped at 10/min to 280. The blood ethanol quantitation was performed by direct injection gas-liquid chromatography on a 6 ft. 10% Carbowax 20 M packed column utilizing flame ionization detection, n-propanol was used as an internal standard.

Analysis of a 0.5 mL heart blood specimen for ethanol showed none detectable at a sensitivity of 0.01 g/dL. Gas chromatography of the basic blood extract revealed the presence of minor concentrations of methamphetamine (120 mcg/L) and amphetamine (50 mcg/L), together with two unidentified constituents. The two unidentified constituents in the basic extract eluted at 1.03 and 1.18 relative to caffeine. The principal constituent, which eluted at 1.03, represented approximately 10× the area of the internal standard. The second, minor, constituent represented approximately 0.4× the area of the internal standard (Fig. 1A). These two constituents were later found to be chromatographically identical with those in a sample of white powder found at the scene of the incident.

Using on-column acetylation, a second 1.0 μL sample of the blood extract, together with an equal volume of acetic anhydride, were submitted to gas-chromatographic analysis under conditions identical to first analysis [*1*]. The principal constituent exhibited a retention time shift appropriate to a primary or secondary amine while the retention time of the minor constituent remained unchanged, indicating no derivatizable functional groups (Fig. 1B).

Data system computer searches of commercial and in-house data bases failed to produce matches consistent with the reactivity and apparent molecular weights of the two compounds. Presumptive identification of the principal constituent, as etryptamine (ethyltryptamine), was finally made with the aid of the Arizona Department of Public Safety Laboratory, by a manual search of an additional bound data base [*2*]. The identity was later confirmed by chromatographic and mass spectral comparison with an authentic sample purchased from Sigma Chemical Company. The total ion chromatograms, structural formula and individual mass spectra are shown in Fig. 2.

Etryptamine was quantitated as the acetyl derivative using the on-column acetylation technique and chromatographic conditions described above for qualitative screening.

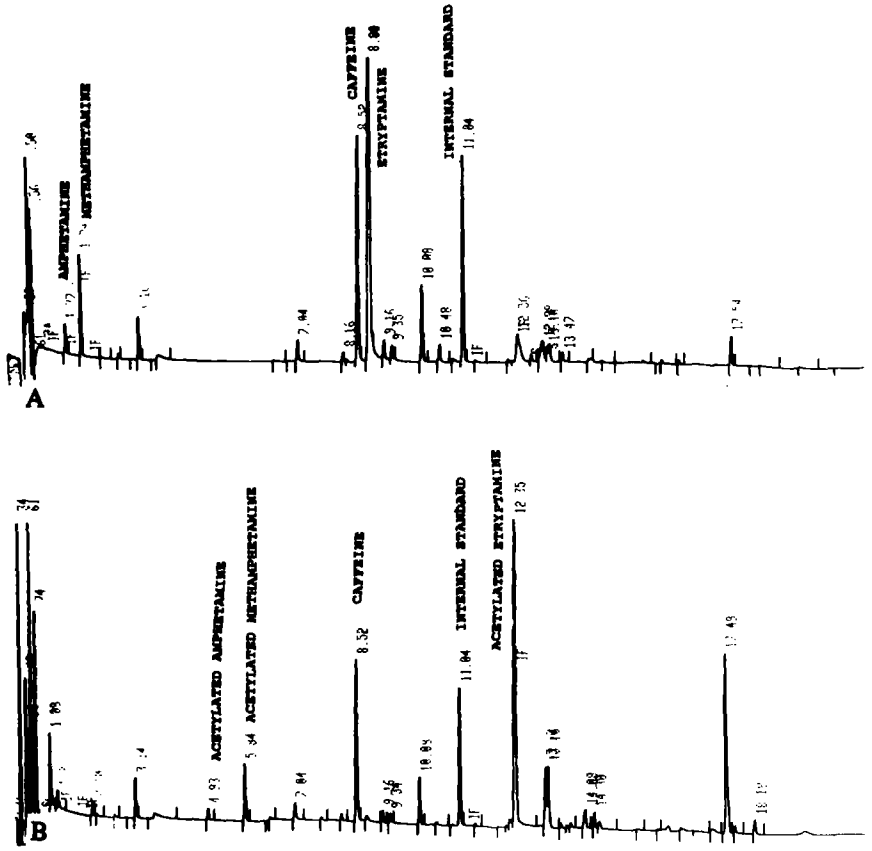

FIG. 1—*(A) Chromatograph of basic extract of 1 mL of blood; (B) Chromatograph of basic extract of 1 mL of blood and acetic anhydride.*

Reduced specimen volumes and dilutions were used to achieve sample concentrations within the linear range of the assay which extended from 0 to 1500 ng/mL. All dilutions were made with deionized water. Table 1 shows etryptamine concentrations of the various tissues and body fluids analyzed. All tissue homogenates were prepared in a Waring laboratory blender.

Discussion and Review of Literature

Early pharmacokinetic studies indicate that etryptamine is rapidly absorbed (t 1/2 abs: 0.62 hours), widely distributed (*V* d: 78.44 L), and eliminated primarily via the kidneys (87%) with a plasma half-life of 8.2 hours. Early studies of etryptamine suggest that it is extensively tissue bound giving rise to a higher than expected volume of distribution. Our study is consistent with these conclusions.

Like other indole derivatives, etryptamine is metabolized principally by 6-hydroxylation. The resulting metabolite, 3-(2-aminobutyl)-6-hydroxyindole, is not believed to be pharmacologically active based on limited animal and in vitro studies [*3,6*]. Reports differ as to the extent of production of the metabolite and the effect of pretreatment (drug loading) but our analyses of hydrolyzed urine failed to demonstrate its presence [*3*].

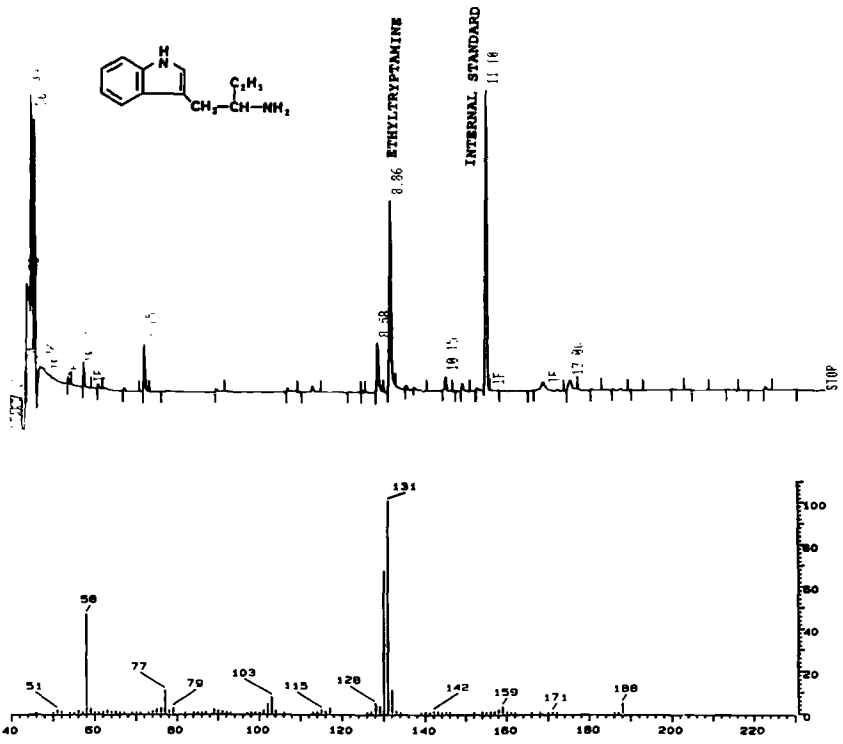

FIG. 2—*Structural formula, total ion chromatogram and mass spectra of etryptamine.*

TABLE 1—*Tissue distribution of etryptamine (in mg/L or mg/kg).*

Specimen	
Blood (heart)	5.6
Liver	18.3
Brain	16.2
Kidney	24.0
Vitreous	2.4
Bile	22.0
Gastric	52.9 (Total)

Etryptamine (ethyl tryptamine; 3-(2-aminobutyl indole) was originally marketed in the U.S. in the late 1950s and early 1960s by the Upjohn Company, under the trade name Monase (etryptamine acetate), a monamine oxidase (MAO) inhibitor. It was promoted as a therapeutic agent for the treatment of depression. Like other MAO inhibitors, etryptamine blocks the metabolism of serotonin and norepinephrine but in addition, it does not effect other enzymes responsible for the formation of serotonin [*3*]. It was, however, removed from the market in March of 1962, for what was termed as an increasing number of instances of agranulocytosis.[2]

Since being removed from the commercial drug market almost 30 years ago, only two published reports of fatal intoxication could be found in the literature. Both of these

[2]Ronald L. Schrock, The Upjohn Company, personal communication.

reports originated in Europe; one in Germany and one in Spain [*4*,*5*]. Inquiries to the local office of the Drug Enforcement Administration and Arizona Department of Public Safety, and nationally to the Drug Abuse Warning Network (DAWN), revealed no documented reports of seizures or intoxications in the United States during the same period.

We believe that this case and its associated data are significant because of the limited information available on this compound and the fact that, as of this writing, it is not a controlled substance. The presence of what we believe is a synthesis by-product also suggests that the compound is being clandestinely produced.

An anecdotal aspect of the search for the reference article describing the synthesis of etryptamine in Chemical Abstracts, at the Arizona State University Library, revealed that this particular paper had been removed. However, information from a witness interrogated by the investigators, suggested this particular sample was synthesized in Oakland, California.

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